



**IN THE CLAIMS:**


Claims 1-18 have been **amended** as follows:

B1  1. (Amended) A method of screening a substance for usefulness in the treatment of a lipid metabolism dysfunction comprising contacting said substance with a ROR receptor, a response element thereof, or a functional equivalent of said receptor or response element, involved in the regulation of the apo C-III gene, and measuring the level of apo C-III gene expression.

2. (Amended) The method according to claim 1, wherein the ROR receptor and the response element of the ROR receptor are the ROR $\alpha$  receptor or the response element of the ROR $\alpha$  receptor.

 3. (Amended) A method of screening a substance for usefulness in the treatment of a lipid metabolism dysfunction, comprising contacting said substance with (a) a receptor of the ROR family involved in the regulation of the expression of the apo C-III gene, (b) a response element of the ROR receptor, (c) a nuclear factor capable of functionally coupling ROR to the RNA polymerase complex, or (d) a functional equivalent of (a)-(c), and then measuring:

- i) the binding of said substance to the ROR receptor or its functional equivalent or the binding of the complex formed by said substance and the ROR receptor to its response element or to a nuclear factor capable of functionally coupling ROR to the RNA polymerase complex; or
- ii) the modulation of the transcriptional activity of a gene placed under the control of a promoter comprising said response element.

 4. (Amended) The method of screening according to claim 3, comprising:

- a) transfecting a cellular host with a DNA fragment encoding an ROR receptor or one of its functional equivalents;
- b) cotransfecting the host in a) with a construct comprising a

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response element of said ROR receptor and at least one reporter gene; and

c) measuring the expression of the reporter gene in the presence of the test substance.

5. (Amended) The method of screening according to claim 3, comprising:

- a) creating a plasmid which comprises several copies of a response element recognized by ROR cloned upstream of a strong heterologous promoter which controls the expression of a reporter gene;
- b) transfecting the construct of a) into host cells which express ROR naturally or artificially;
- c) incubating the host cells of b) in the presence of the test substance; and
- d) measuring the activity of the reporter gene.

6. (Amended) The method of screening according to claim 3, comprising:

- a) creating a plasmid which comprises several copies of a response element recognized by ROR cloned upstream of a promoter which controls the expression of a selectable gene;
- b) transfecting the construct of a) into a cellular host;
- c) cotransfecting the host of b) with the aid of a vector expressing ROR;
- d) incubating the host of c) in the presence of the test substance; and
- e) measuring the cellular survival of said cellular host in the presence of a toxic prodrug.

7. (Amended) The method of screening according to claim 3, comprising:

- a) creating a plasmid which comprises several copies of a response element recognized by the yeast nuclear factor Gal4 cloned upstream of a strong promoter which controls the activity

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of a reporter gene;

- b) creating a plasmid from a chimera which comprises the DNA binding domain of Gal4 and the DEF domains of ROR which are the ROR domains to which the ligands bind;
- c) cotransfecting the plasmids in a) and b) into a cellular host;
- d) incubating the host of c) in the presence of a test substance; and
- e) measuring the activity of said reporter gene.

8. (Amended) The method of screening according to claim 3, comprising:

- a) transforming the cellular host with a construct carrying a gene encoding the ROR receptor or its functional equivalent or a response element of the ROR receptor, and;
- b) assaying said cellular host or an extract thereof for the competitive displacement in the binding of labelled and unlabeled ligand to said ROR receptor.

9. (Amended) The method of screening according to claim 4, wherein the construct carrying the gene encoding the ROR receptor or a response element of the ROR receptor also comprises a reporter gene.

10. (Amended) The method of screening according to claim 9, wherein the reporter gene is chosen from chloramphenicol acetyltransferase, the gene for luciferase from firefly or from Renilla, the gene for secreted alkaline phosphatase, the gene for beta-galactosidase or the gene for apo C-III.

11. (Amended) The method of screening according to claim 4, wherein the cellular host is chosen from mammalian cells, bacteria, yeasts, or insect cells.

12. (Amended) The method of screening according to claim 3, wherein the effect of said substance on the expression of said apo C-III gene is determined using transfection or analysis of mRNAs *in vitro* or on models *in vitro* or *in vivo*.

13. (Amended) The method of screening according to claim 3, wherein the ROR receptor and the response element of the ROR receptor are the ROR $\alpha$  receptor and the response element of the ROR $\alpha$  receptor.

14. (Amended) A method for preparing a pharmaceutical composition or a medicament useful in treating or preventing atherosclerosis in humans or animals comprising selecting a substance screened according to claim 3.

15. (Amended) A method for treating or preventing atherosclerosis in humans or animals comprising modulating the expression of apo C-III using a medicament or a pharmaceutical composition comprising a substance selected according to claim 3.

16. (Amended) A method for treating or preventing atherosclerosis in humans or animals comprising administering a medicament or a pharmaceutical composition comprising a substance capable of binding to the ROR receptor, its response element, or a functional equivalent thereof involved in the regulation of the apo C-III gene.

17. (Amended) The method according to claim 3, wherein the substance has antiatherosclerotic properties.

18. (Amended) A method of screening according to claim 8, wherein the construct carrying a gene encoding the ROR receptor or a response element of the ROR receptor also comprises a reporter gene.

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Please add the following new claims:

--19. The method according to claim 1, wherein the lipid metabolism dysfunction is atherosclerosis.

20. The method according to claim 2, wherein the lipid metabolism dysfunction is atherosclerosis.

21. The method of screening according to claim 4, wherein the lipid metabolism dysfunction is atherosclerosis.

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22. A method of regulating the expression of the apo C-III gene, comprising contacting a substance with the receptor of the ROR family or a response element of the ROR receptor involved in the regulation of the expression of the apo C-III gene or a response element of the ROR receptor or a nuclear factor capable of functionally coupling ROR to the RNA polymerase complex, or a functional equivalent thereof, and then measuring:

- i) the binding of said substance to the ROR receptor or its functional equivalent or the binding of the complex formed by the said substance and the ROR receptor to its response element or to a nuclear factor capable of functionally coupling ROR to the RNA polymerase complex; or
- ii) the modulation of the transcriptional activity of a gene placed under the control of a promoter comprising the said response element. --

#### REMARKS

#### The Rejection of the Claims Under 35 U.S.C. §112, Second Paragraph Should Be Withdrawn

Claims 1, 3, 8 and 14-17 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Claims 1, 3, 8 and 14-17 have been rewritten for better clarity. The "and/or" language has been replaced with "or".

Claims 1, 2 and 14-17 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite and vague. These claims have been rewritten to conform with a proper method claim format consistent with U.S. claim drafting practice.

Claims 3-7, 8 and 12 stand rejected as well for being indefinite and vague. Claims 3-7 and 12 have been rewritten to remove the indefinite language of 'an appropriate means'. Claim 8 has been rewritten to better clarify the binding test. The scope of the claim remains unchanged.